

the skin covering the ipsilateral breast (i.e., a 5 mm width segment on the breast surface). Treatment plans with EBB were performed and compared to stereotactically guided DCAT. Dose-volume histograms (DVHs) were compared in both treatment techniques. The V90(PTV) (volume of the PTV that received 90% of the prescribed dose), the V50(OARs) (volume of the OARs that received 50% of the prescribed dose), a conformity index (CI), and an inhomogeneity coefficient (IH) were calculated in both techniques. **Results:** Five tumors were located in the left breast, and five in the right one. Three were located superficially (up to 4 cm), and seven were deeply located (>4 cm). The mean CTV and PTV volume were 33.7 cc (range 6.0–79.6), and 109.2 cc (range 48.7–206.0), respectively. The mean coverage of the PTV by the 90% isodose was 94.6% for DCAT, and 92.4% for EBB. The mean minimal and maximal dose to the PTV were 13.5 Gy (range 12.8–13.9), and 17.7 Gy (range 16.0–19.9) for DCAT, and 10.2 Gy (range 8.0–13.8), and 16.8 Gy (range 16.1–17.8), for EBB. The mean V50(OARs) for DCAT and EBB were: ipsilateral breast: 215.1 cc and 239.6 cc; ipsilateral lung: 12.9 cc and 145.32 cc; skin: 23.0 cc and 31.9 cc; and heart: 0 cc and 14 cc respectively. The mean CI value was 1.28 for DCAT and 2.43 for EBB. The mean IH value was 0.30 for DCAT and 0.72 for EBB.

Conclusions: Compared with electron beams, stereotactic guided DCAT with 6 MV x-ray beams may be preferred especially for deeply located breast tumors growing close to the chest wall. A marked OARs dose-sparing effect was observed, in addition to potential improvement in cosmesis after treatment.

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POSTER

Adjuvant therapy for early stage breast cancer (EBC): distant disease-free survival (DDFS) as a predictor of overall survival (OS)

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Background: OS advantages are often difficult to demonstrate in trials evaluating treatment for EBC, as this requires long follow-up (FU) and large trials. Results are also confounded by factors such as further treatment. DFS, the primary end point in many adjuvant trials, is not a consistent predictor of OS, and lack of standard definitions renders its interpretation difficult. A better, quicker end point is needed as a surrogate for OS. Distant metastases (DM), the most common type of recurrence, are responsible for the initial peak of relapse seen at 2 years post surgery and are associated with the highest risk of death compared with locoregional and contralateral events. The sites of distant relapse also affect outcome; patients with bone metastases fare better than patients with visceral disease. As reductions in DM are likely to improve outcomes, DDFS may be a better short-term OS predictor.

Methods: The impact of common adjuvant therapies (chemotherapy [CT], tamoxifen [TAM], and aromatase inhibitors [AIs]) on DM risk and OS were examined.

Results: CT trials show that improvements in DDFS often precede subsequent improvements in OS. In NSABP B14, TAM significantly improved DDFS at 4 years and OS at 10 years. In ATAC and BIG 1–98, over half of EBC recurrences are DM, but OS differences are limited by short FU. Visceral relapse was the most common site of distant relapse in BIG 1–98. Letrozole therapy significantly reduced DM risk, resulting in fewer soft tissue, bone, and visceral metastases when compared with TAM. ATAC showed no significant reduction in DM risk with anastrozole in hormone receptor-positive patients. The reason for this difference is unclear. The IES initially showed a significant reduction in DM risk, but the number of events at specific sites was not reported. Upon longer FU, a borderline significant benefit in OS in the estrogen receptor-positive/unknown subgroup favoring exemestane was seen.

Conclusion: Several adjuvant trials show that improvements in DDFS often precede significant improvements in OS. AIs show superiority over TAM in reducing DM risk (IES, BIG 1–98) in all sites of recurrent disease. DDFS may be a better, more achievable end point than OS for women with EBC and could hasten the development of future adjuvant breast cancer therapies.

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POSTER

Endocrine effects of adjuvant letrozole plus triptoreline versus tamoxifen plus triptoreline in premenopausal patients with early breast cancer

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Background: We are conducting a phase 3 trial (Hormonal adjuvant treatment Bone Effects – HOBEO) in patients with early breast cancer, comparing Tamoxifen (Tam), Letrozole (L) and L + Zoledronate (Z) for the effect on bone mineral density at 1 year. Postmenopausal and premenopausal patients are eligible, the latter also receiving monthly triptorelin (Tr). The aim of the present study is to describe endocrine effects of 6 months of adjuvant treatment with L plus Tr in premenopausal early breast cancer patients and to compare such effects with those of 6 months of Tam plus Tr.

Patients and Methods: Prospectively collected hormonal data were available for 81 women, of whom 30 have been assigned to receive Tam+Tr and 51 to L+Tr±Z, assuming that Z has no endocrine effects. Serum 17- β -estradiol, FSH, LH, D4-androstenedione, testosterone, dehydroepiandrosterone-sulphate, progesterone, ACTH and cortisol are measured at baseline and after 6 months of treatment. We compared, for each hormone, 6-months values between treatment groups, by applying Exact Wilcoxon-Mann-Whitney test. Differences between 6-months and baseline values have not been calculated to avoid dilution due to chemotherapy-induced postmenopausal values.

Results: There were no differences in change of plasma levels of testosterone, progesterone, ACTH, androstenedione, and dehydroepiandrosterone between the two groups. Significant differences are reported in the table ($p < 0.05$).

Hormone	Median value (range)		p value
	Treatment arm		
	Tam+Tr	L+Tr (±Z)	
Estradiol pg/ml	7.95 (<5–43.9)	4.9 (<5–24.5)	0.0008
FSH mUI/ml	2.65 (0.9–26.5)	10.8 (2.2–131.1)	<0.0001
LH mUI/ml	0.3 (0.1–1.2)	0.2 (0.1–0.8)	0.0005
Cortisol µg/d ^a	18.45 (4.6–30.3)	10.5 (5.3–17.9)	<0.0001

^aMedian cortisol serum levels were within normal range in both groups.

Conclusions: These data suggest that letrozole in combination with triptorelin, induces a more intense estrogen suppression also in premenopausal patients, as compared to tamoxifen. Such evidence makes reasonable the hypothesis that the higher efficacy of letrozole versus tamoxifen shown in postmenopausal patients could be confirmed also in premenopausal patients.

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POSTER

Tantalum and titanium surgical clips as fiducial markers for breast radiotherapy in a tissue equivalent phantom

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Background: Surgical clips are used to facilitate image guided 3D conformal radiotherapy for breast cancer. This study was designed to determine which clip type: medium tantalum (MTa), small tantalum (STa), medium titanium (MTi) or small titanium (STi), can best be visualised in a tissue equivalent phantom, using different imaging modalities.

Materials and Methods: The visibility of each clip type in each breast quadrant was graded by three blinded observers for BrainLAB ExacTrac floor mounted kilovoltage (kV), isocentric kV, and isocentric megavoltage (MV) imaging modalities. A three point grading system was used: "clearly visible", "some uncertainty" and "not visible". Binomial logistic regression and pairwise comparisons were used for analysis. For computed tomography (CT), the volume of artifact generated by each clip type in the phantom was determined at different slice and index thickness.

Results: MTa clips were best visualised (MTa > STa > MTi > STi, $p < 0.0001$). The visibility for different clip materials, sizes and locations was

compared: tantalum > titanium ($p < 0.0001$), medium > small ($p < 0.0001$), and lower outer > other quadrants ($p = 0.004$). For floor mounted kV imaging, 98.4% MTa, 91.1% STa, 53.1% MTi, and 10.4% STi clips were clearly visible. For isocentric kV imaging, 99.0% MTa, 93.8% STa, 88.9% MTi, and 61.8% STi clips were clearly visible. For isocentric MV imaging, 94.8% MTa, 36.1% STa, 0% MTi, and 0% STi clips were clearly visible. The mean volume (cm^3) of artifact generated by MTa, STa, MTi, and STi clips was 0.81, 0.23, 0.07, and 0.01, respectively.

Conclusions: MTa clips were visualised best, but their CT artifact was unacceptable. STi clips were poorly visualised. Both MTi and STa clips proved suitable as fiducial markers for isocentric kV imaging, although MTi clips generate less CT artifact. STa clips were best visualised for floor mounted kV imaging.

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POSTER

Incidence of chemotherapy induced amenorrhea and the role of hormone therapy on ovarian function in hormone sensitive breast cancer

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Background: The incidence of chemotherapy-induced amenorrhea (CIA) and the importance of ovarian function (OF) in hormone sensitive breast cancer is not well defined. The aim of this study is to define the risk factors of permanent amenorrhea after chemotherapy in premenopausal patients, and the impact hormonal therapy has in OF.

Material and Methods: 323 premenopausal patients from our center, diagnosed with hormone sensitive (ER and/or PR positive) invasive breast carcinoma between January 1998 and June 2005 were selected. All received adjuvant or neoadjuvant anthracycline based chemotherapy, with or without taxanes, or high dose chemotherapy followed by autologous bone marrow transplantation (ABMT). The kind of hormone treatment received was also taken into consideration. The data was obtained from the medical records. The two main questions were the incidence of CIA among our patients according to the patient's age and chemotherapy schedule, and the restart of the OF during hormonal treatment.

Results: 255 pts with CIA, and 68 with no amenorrhea, were analyzed. The age distribution among patients with CIA was as follows: 45 yrs or older: 140 patients (95.2%), 40–45 yrs: 66 patients (71.74%), 35–40 yrs, 41 patients (61.1%), 35 yrs or younger: 8 patients (36.3%), $p < 0.0001$. A significant difference in CIA was found between the two groups ($p < 0.034$). 160 out of 212 patients in the anthracycline based chemotherapy group was found to have CIA (75.4%), while this was the case in 77 of 93 patients in the anthracycline and taxane group (82.8%) There was 100% amenorrhea in the group of 17 patients that received high dose chemotherapy followed by ABMT.

Of 148 patients with CIA and tamoxifen, 10 recovered OF: 7 were still on tamoxifen (4.7%), 3 patients had discontinued treatment (2%). Of 107 on aromatase inhibitors, 7 recovered OF (6.5%)

Conclusions: There is a direct correlation between the patients' age and chemotherapy schedule combining anthracycline and taxanes, and chemotherapy-induced amenorrhea. Aromatase inhibitors treatment was associated with a higher recovery rate of ovarian function.

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POSTER

Breast ductal lavage biomarkers in relation to estrogen response and risk factors

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Background: The importance of estrogen in breast cancer risk is amply confirmed by clinical data on the effectiveness of selective estrogen receptor modulators and aromatase inhibitors, yet measurements of plasma estrogen concentrations have not provided the expected degree of association with breast cancer incidence. This disparity may be explained by the poor correlation between plasma and breast fluid concentrations of estrogens and products of estrogen action. The present study provides an estimate of the association between a number of factors measured in ductal lavage fluid and risk as assessed by the Gail model.

Methods: Women at high risk for breast cancer were recruited (Gail score for 40 premenopausal women: 1.6–6.9, median 2.5; for 27 postmenopausal: 1.6–6.9, median 3.0). Ductal lavage was performed prior to treatment with tamoxifen. The cells were removed and the fluid was reduced to a volume of 1.0 ml for immunoassays of estradiol, estrone sulfate, androstenedione, DHEA, cathepsin D, and EGF. Significant factors from backward stepwise multiple regression for each group were determined after normalization by log transformation

Results: In premenopausal women with Gail score as the dependent variable, the model R2 was 0.207; estrone sulfate had a standard coefficient

of 0.506 ($p = 0.003$) and EGF had a standard coefficient of -0.464 ($p = 0.008$). Other factors did not reach significance. In postmenopausal women with Gail score as the dependent variable, the model R2 was 0.356. EGF had a standard coefficient of 0.753 ($p = 0.003$) and DHEA had a standard coefficient of -0.524 ($p = 0.048$). Other factors did not reach significance. Cathepsin D was related to estrone sulfate in post- but not premenopausal patients. R2 was 0.243, and the standard coefficient was 0.493 ($p = 0.002$).

Conclusions: Gail scores in women at high risk for breast cancer are highly significantly related to components of breast fluid but the associations were quite different in pre- and postmenopausal women. An estrogen was an important predictor of risk in premenopausal women and EGF was the most important predictor of risk on postmenopausal women. The estrogen response protein, cathepsin D, was not related to estrogen in the same manner as risk.

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POSTER

Acute effects on cardiac function after breast radiotherapy – a strain rate imaging study

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Background: Radiotherapy for breast cancer is associated with long-term cardiac dysfunction. Doppler Myocardial Imaging (DMI) has been shown to be a sensitive echocardiographic tool for quantifying subtle changes in cardiac function. This study investigates the occurrence of early radiation-induced changes in regional cardiac function by DMI.

Materials and Methods: In a pilot study, 15 women (age 54 ± 14.4 years) with left-sided breast cancer were examined. All patients received radiotherapy to the breast or chest wall by respectively tangential photon beams or direct electron fields. In 8 patients, the internal mammary and medial supraclavicular (IM-MS) lymph nodes were treated by direct anterior mixed photon and electron beams. Dose prescription was 50 Gy in 25 fractions. In all patients, part of the cardiac apex was irradiated. Patients with an intact breast received an additional boost to the tumour bed of 16 Gy. Epirubicin containing chemotherapy was given to 9 patients prior to radiotherapy. Standard echocardiography and DMI data were obtained before and after radiotherapy. Peak systolic longitudinal velocity (VEL) and strain rate (SR) as well as systolic strain (S) were measured in all patients for the 18 mid, basal and apical left ventricular (LV) segments.

Results: Conventional and DMI data could be obtained in all patients before and after radiotherapy. LV dimensions, ejection fraction and other conventional parameters of systolic and diastolic function did not change after radiotherapy. Segmental VEL was also not different. In contrast, a significant reduction in S (21.5 ± 7.3 to 17.8 ± 7.6 , $p = 0.001$) and SR (1.41 ± 0.52 to 1.17 ± 0.41 , $p = 0.001$) was found after treatment only at the level of apical segments, but not in the basal or mid segments (-21.1 ± 6.1 to -20.0 ± 6.5 and -1.50 ± 0.40 to -1.40 ± 0.34 , resp., both n.s.).

Conclusions: In contrast to conventional echocardiography, myocardial deformation parameters allowed the detection of regional decrease in myocardial function early after radiotherapy for left-sided breast cancer. Further follow up is needed to assess the relation between these early changes and long term dysfunction.

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POSTER

MR Imaging in the preoperative assessment of patients with lobular carcinoma of the breast

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Background: Infiltrating lobular carcinoma is the second most common breast malignancy and represents 7–15% of the invasive breast cancers. The diagnosis is however not without difficulties.

Lobular carcinoma shows a diffuse growth pattern of cellular infiltration, including linear file arrangement and a lack of desmoplastic reaction, necrosis or calcification. These typical histological characteristics may account for the existing imaging difficulties. Tumour extent can be underestimated on mammography and ultrasound or multifocal disease can be missed.

In this study we retrospectively compared findings on preoperative MR imaging with mammography and US in 35 patients with lobular carcinoma and evaluated the effect on the surgical therapy.

Methods: 35 patients who were diagnosed with a lobular carcinoma between december 2003 and december 2006 and underwent pre-operative MR imaging were included. Two radiologists retrospectively reviewed all